two different structures. 1H-NMR studies have shown that either structure is characterized by specific sets of salt bridges formed between residues on both αβ dimers, the so-called α1β2 (or α2β1) interdimeric interactions. The accepted consensus states that the structural change consists of a ~15°rotation of one dimer over the other when converting from ''T'' to ''R'', and vice versa, whereas the αβ dimers themselves do not experience any conformational change, i.e., the α1β1 (or α2β2) interface remains unaltered. Functionally, ''T'' and ''R'' are characterized by low and high affinity for the ligand, respectively.
In the present work, we have altered chemically this allegedly inert intradimeric α1β1 interface and found striking functional changes that cannot be explained in terms of the canonical allosteric model, yet ''T'' and ''R'' structural traits were unequivocally present. This finding exemplifies the functional versatility that a protein can attained, exceeding the limits of what is called ''of physiological significance''. Experimental data that support this finding will be presented.

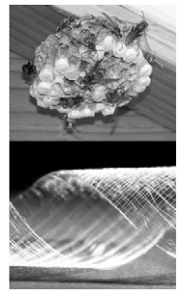
244-Pos Board B13
The Effect of Small Regulatory RNA on Globular Protein Aggregation
Jeremiah Babcock, Lorenzo Brancaleon.
University of Texas at San Antonio, San Antonio, TX, USA.
Small regulatory RNA segments, such as microRNA (miRNA) or silencing RNA (siRNA) binding to proteins could effect the association mechanisms of protein aggregation. Extended protein aggregation, known as fibrillization, has links to degenerative diseases like Alzheimers or prion disease. The formation of fibrils is thought to be a non-specific property of proteins, and can be demonstrated with well-known model globular proteins like serum albumin, lysozyme, beta-lactoglobulin and the like. Much research has been devoted to this field, but with the recent discovery of micro/silencing RNA, small regulatory RNA generally less than 70 base pairs, the question arises on the effect of these nucleic acids on the aggregation process behind fibril formation. Therefore, this study attempted for the first time to probe two effects in the fibrillization process: first, the binding affinity of the selected microRNA MIR106A to the model proteins lysozyme and bovine serum albumin in fibril forming conditions, and second, the long-term effect of the protein-nucleic acid complex on the fibril formation process. Fluorescence spectroscopy, to include time-resolved anisotropy decay of fluorescein or dansyl-labeled complexes, and sizing techniques like atomic force microscopy to track aggregation patterns were incorporated.

245-Pos Board B14
Clarifying Alpha Crystallin Chaperone Function by using an Insulin B-Chain Aggregation Model
Karen W. Cheng, Raysa G. Cabrejo, Alexander H. Pearlman,
James A. Hebda, **Patricia B. O'Hara**.
Amherst College, Amherst, MA, USA.
The crystallin family of proteins exist in high concentrations in the lens of the eye by are also found throughout the body. In the lens, alpha-crystallin isoforms A and B exist in a ratio of 2 to 3. Their role in the eye is to provide a structural matrix and prevent protein misfolding. The inducible aggregation of the insulin-B chain serves as a model to the protein aggregation that occurs in the human lens over time. This protein aggregation contributes to lens opacity, which is the beginning of cataract formation. In this study, we explore the kinetic and thermodynamics of such system in order to understanding the mechanism of alpha-crystallin chaperone function in insulin aggregation. Insulin aggregation can be measured through light scattering. Our preliminary result suggest a mechanism for aggregation in which a B-chain insulin dimer formation precedes aggregation and that alpha crystallin and insulin monomer form a 2 to 1 complex that inhibits this aggregation. Thermodynamic and kinetic constants will be presented for the purified alpha chrystallins as well as mixtures and bulk protein.

246-Pos Board B15
Structural Metal Mediated Self Assembly of Collagen Mimetic A:B:C Heterotrimer Peptides into Higher Oder Structures
Avanish S. Parmar[1,2], **Nida F. Hasan**[1,3], Vikas Nanda[1,2].
[1]CABM, UMDNJ, Piscataway, NJ, USA, [2]CABM, Rutgers University, Piscataway, NJ, USA, [3]University of Maryland, College Park, MD, USA.
Collagen is the most abundant protein in the human body with many favorable properties making it an attractive target for biomaterials. Currently, animal derived collagens are utilized in biomedical, cosmetics and for other applications. But, they are costly to purify and risk of prior contamination. Synthetic collagen can overcome some of these issues and potentially allow greater control of material properties. Recently, collagen like homotrimer peptides has been utilized to form metal trigger higher order structures. In this study we present the case of a higher order structure formed by heterospecific A:B:C collagen like peptides using a structural metal. Here using electrostatic interactions in conjunction with the metal binding site to drive the formation of higher order assembly of heterotrimer collagen like peptide. The assembled structures range from particle to fibers to disks. We hypothesize that using these heterotrimer peptides will allow control over the higher order structures and chemical functionality of biomaterials. Also, the insight gain from this study will help to improve the molecular design of biomimetic materials.

247-Pos Board B16
Aggregation of Trp>Glu Mutants of the Human Gamma-D Crystallin: A Model for Hereditary or UV-Induced Cataract
Eugene Serebryany[1,2], Nathaniel Schafheimer[1], Susan L. Lindquist[1,2], Jonathan A. King[1].
[1]MIT, Cambridge, MA, USA, [2]Whitehead Institute, Cambridge, MA, USA.
Cataract is a protein misfolding disorder resulting from formation of light-scattering aggregates of proteins from the crystallin family. These long-lived proteins account for 90% of all protein in the human eye lens. The γD crystallin consists of two symmetrical domains, each of which has a duplicated Greek key fold. Maintaining this topologically complex native fold of the γD crystallin is essential for lens transparency. A number of point mutants in the γD crystallin gene cause early-onset cataract. UV-B exposure accelerates cataract onset, and UV irradiation of purified wild-type γD results in aggregation in vitro. A distinctive feature of the Greek key fold is the presence of highly conserved buried tryptophans. Replacements of tryptophan by charged glutamate groups may represent a model of UV-induced photodamage – introduction of a charged group into the hydrophobic core generating ''denaturation from within.'' We show that such Trp>Glu mutants can display vastly increased aggregation propensity under physiological conditions *in vitro*. Furthermore, a striking property of these mutants is their ability to drive the wild-type protein into the aggregated state. Domain swapping mechanisms can account for this aggregation behavior.

248-Pos Board B17
Artificial Honeybee Silk: A Recombinant Protein as a Biomimetic Structural Material
Jeffrey S. Church[1], Mickey G. Huson[1], Tara D. Sutherland[2].
[1]CSIRO Materials Science and Engineering, Belmont, Australia, [2]CSIRO Ecosystem Sciences, Acton, Australia.
Honeybee larvae produce silken cocoons that provide mechanical stability to the hive. The silk proteins are small and non-repetitive and therefore can be produced at large scale by fermentation in *E. coli*. Recombinant silk proteins which have a coiled coil structure can be fabricated into a range of forms including sponges and fibers. The resultant material is soluble in water and requires a post-production stabilizing treatment. Aqueous methanol treatment induces the formation of a stabilizing ß-sheet structure, with the amount of ß-sheet being controlled by time or methanol concentration. Dry heat treatment at 190°C also produces a water insoluble material but without significant secondary structural changes. Honeybee silk proteins are particularly high in lysine, serine, threonine, glutamic acid and aspartic acid. The stability of the heat treated material is attributed to the generation of covalent cross-links including lysinoalanine and isopeptide groups. The unique ability to stabilize material by controlling secondary structure rearrangement and covalent cross-linking allows us to design recombinant silk materials with a wide range of properties and potential applications.



249-Pos Board B18
Self-Replicating Amyloid-Beta Oligomers Open Doors to New Molecular Mechanisms in Alzheimer Disease
Vijay Rangachari[1], Amit Kumar[1], Lea Paslay[1], Daniel Lyons[2], Sarah Morgan[1], John Correia[2].
[1]University of Southern Mississippi, Hattiesburg, MS, USA, [2]University of Mississippi Medical Center, Jackson, MS, USA.
Aggregates of amyloid-β (Aβ) peptides have been implicated in the etiology of Alzheimer disease (AD). Among the different forms of Aβ aggregates, low molecular weight species ranging between 2- and 50-mers, also called ''soluble oligomers,'' have emerged as the species responsible for early synaptic dysfunction and neuronal loss. Emerging evidence suggests that the neurotoxic oligomers need not be formed along the obligatory nucleation-dependant fibril formation pathway. In our earlier work, we reported the isolation of one such ''off-pathway'' 12–18-mer species of Aβ42 generated from fatty acids called large fatty acid-derived oligomers (LFAOs) (Kumar, A., Bullard, R. L., Patel, P., Paslay, L. C., Singh, D., Bienkiewicz, E. A., Morgan, S. E., and Rangachari,